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In re Application of:

Applicant	:	Hans-Henrik Ipsen et al.
Serial No.	:	10/085,768
Filed	:	February 26, 2002
For	:	METHOD OF DETECTING AN ANTIBODY IN A LIQUID SAMPLE
Art Unit	:	1641
Attorney Docket No.	:	478.1.012 DIV

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO: COMMISSIONER OF PATENTS AND TRADEMARKS, WASHINGTON D.C. 20231
ON April 2, 2002
NAME Jill S. Garretson
SIGNATURE Jill S. Garretson

Commissioner of Patents
Washington, D.C. 20231

April 2, 2002

PRELIMINARY AMENDMENT

Dear Sir:

Please amend the application as follows.

IN THE SPECIFICATION:

Please replace paragraph 1 on page 1 with the following new paragraph 1.

04/18/2002 RWEBRAHT 00000041 10085768

01 FC:103 396.00 OP
02 FC:102 84.00 OP

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Line By Line Specification:

The present application is a divisional application of U.S. Serial No. 09/339,545 filed June 24, 1999 which claims the priority benefits of Danish Patent Application Serial No. PA1998/00821 filed June 24, 1998. The present invention relates to a method of detecting a specific antibody in a liquid sample.

Full Text Amendment:

The present application is a divisional application of U.S. Serial No. 09/339,545 filed June 24, 1999 which claims the priority benefits of Danish Patent Application Serial No. PA1998/00821 filed June 24, 1998. The present invention relates to a method of detecting a specific antibody in a liquid sample.

Please replace the second full paragraph 2 on page 3 with the following new paragraph 2.

Line By Line Amendment:

This first object is achieved with the method of the invention, [a first aspect of which is defined in claims 1-6,] the essential new feature of the invention being that an additional sequence of separation and washing of the intermediate solid phase complex consisting of particle with reactant antibody and sample antibody is carried out prior to addition of ligand.

Full Text Amendment:

This first object is achieved with the method of the invention, the essential new feature of the invention being that an additional sequence of separation and washing of the intermediate solid phase complex consisting of particle with reactant antibody and sample antibody is carried out prior to addition of ligand.

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Please replace third full paragraph on page 4 with the following new paragraph 3.

Line By Line Amendment:

This second object is obtained by [with the second aspect of the invention, which is defined in claim 7-12. According to this aspect the level,] the nature and the temporal development of the interference between different types of immunologically active serum components, e.g. antibodies, are used as parameters for evaluating/predicting the effect of a Specific Allergy Vaccination treatment. Thus, it has surprisingly been found that the said parameters hold valuable information about the immunological status of a person as well as the response of a person to a selected treatment scheme.

Full Text Amendment:

This second object is obtained by the nature and the temporal development of the interference between different types of immunologically active serum components, e.g. antibodies, are used as parameters for evaluating/predicting the effect of a Specific Allergy Vaccination treatment. Thus, it has surprisingly been found that the said parameters hold valuable information about the immunological status of a person as well as the response of a person to a selected treatment scheme.

Please replace paragraph 1 on page 5 with the following new paragraph 1.

Line By Line Amendment:

The third object of the invention is obtained [with the third aspect of the invention, which is defined in claims 20-31. According to this aspect the level,] by the nature and the temporal development of the interference between different types of immunologically active serum components, e.g. antibodies, are used as a parameter for evaluating the immunological status of a subject, in particular evaluating/predicting the effect of allergy treatment, allergy vaccination treatment or Specific Allergy Vaccination treatment.

Thus, it has surprisingly been found that the said parameter hold valuable information about the immunological status of a person as well as the response of a person to a selected treatment scheme.

Full Text Amendment:

The third object of the invention is obtained by the nature and the temporal development of the interference between different types of immunologically active serum components, e.g. antibodies, are used as a parameter for evaluating the immunological status of a subject, in particular evaluating/predicting the effect of allergy treatment, allergy vaccination treatment or Specific Allergy Vaccination treatment. Thus, it has surprisingly been found that the said parameter hold valuable information about the immunological status of a person as well as the response of a person to a selected treatment scheme.

Please replace paragraph 3 on page 5 with the following new paragraph 3.

Line By Line Amendment:

The fourth object of the invention is obtained [with the fourth aspect of the invention, which is defined in claims 32-35. This aspect of the invention is] based on the recognition that the measurement obtained with the subassays 1, A and C [(see claims 20, 21 and 29, respectively)], i.e. a measurement, which is carried out in the presence of interfering factors in the sample, is particular useful for evaluating the effect of allergy treatment, allergy vaccination treatment and Specific Allergy Treatment (SAV). Thus, the measurement obtained with this method is obtained under conditions, which correspond to in vivo conditions, and hence is a more physiological and clinical relevant measurement for evaluating treatment effects.

Full Text Amendment:

The fourth object of the invention is obtained based on the recognition that the measurement obtained with the subassays 1, A and C, i.e. a measurement, which is carried out in the presence of interfering factors in the sample, is particular useful for evaluating the effect of allergy treatment, allergy vaccination treatment and Specific Allergy Treatment (SAV). Thus, the measurement obtained with this method is obtained under conditions, which correspond to in vivo conditions, and hence is a more physiological and clinical relevant measurement for evaluating treatment effects.

Please replace the third full paragraph on page 7 with the following new paragraph 3.

Line By Line Amendment:

Most prior art "quantitative" IgE assays measure IgE in the absence of competing substances. The present invention describes the measurement of IgE in the presence and absence of any (serum originating) competing substance. Thus, the methods [defined] referred to in [claims 1-6 (cf.] Figures 2a-c[)] measure IgE in the absence of competing agents, whereas the method defined in step (i'), (i), (i''), (y'), (y) and

Full Text Amendment:

Most prior art "quantitative" IgE assays measure IgE in the absence of competing substances. The present invention describes the measurement of IgE in the presence and absence of any (serum originating) competing substance. Thus, the methods referred to in Figures 2a-c measure IgE in the absence of competing agents, whereas the method defined in step (i'), (i), (i''), (y'), (y) and

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Please replace the first line on page 8 with the following new first line.

Line By Line Amendment:

(y") [of claims 7-12], respectively, measure IgE in the presence of competing agents.

Full Text Amendment:

(y"), respectively, measure IgE in the presence of competing agents.

Please replace the second full paragraph on page 8 with the following new paragraph 2.

Line By Line Amendment:

In the second aspect of the invention [(Claims 7-12)], two subassays are used in the method, viz. subassays, wherein the reaction between sample antibody and allergen is effected in the absence (subassay (h'), (h), (h"), (x'), (x) and (x")) and presence (subassay (i'), (i), (i"), (y'), (y) and (y") of the other sample constituents, respectively.

Full Text Amendment:

In the second aspect of the invention, two subassays are used in the method, viz. subassays, wherein the reaction between sample antibody and allergen is effected in the absence (subassay (h'), (h), (h"), (x'), (x) and (x")) and presence (subassay (i'), (i), (i"), (y'), (y) and (y") of the other sample constituents, respectively.

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Please replace Fig. 2a-c on page 13 with the following new Fig. 2a-c.

Line By Line Amendment:

Fig. 2a-c are diagrammatic representations of three preferred assays [suitable for use in the methods defined in claims 7-9 (submethods)] of the present invention.

Full Text Amendment:

Fig. 2a-c are diagrammatic representations of three preferred assays of the present invention.

Please replace the third paragraph on page 15 with the following new paragraph 3.

Line By Line Amendment:

Figure 2a shows a preferred embodiment [(claim 2)] of the second aspect of the invention, wherein components (i) and (ii) are mixed and incubated to form a two-component complex, which is washed. The component (iii) is added to form a three-component complex, after which component (iv) is added to form a four-component complex, which is washed and subjected to chemiluminescence measurement.

Full Text Amendment:

Figure 2a shows a preferred embodiment of the second aspect of the invention, wherein components (i) and (ii) are mixed and incubated to form a two-component complex, which is washed. The component (iii) is added to form a three-component complex, after which component (iv) is added to form a four-component complex, which is washed and subjected to chemiluminescence measurement.

Please replace the fourth full paragraph on page 15 with the following new paragraph 4.

Line By Line Amendment:

Figure 2b shows another preferred embodiment [(claim 5)] of the second aspect of the invention, which corresponds to that shown in Figure 2a except that components (iii) and (iv) are added in one operation.

Full Text Amendment:

Q12

Figure 2b shows another preferred embodiment of the second aspect of the invention, which corresponds to that shown in Figure 2a except that components (iii) and (iv) are added in one operation.

Please replace the fifth full paragraph on page 15 with the following new paragraph 5.

Line By Line Amendment:

Figure 2c shows a further preferred embodiment [(claim 6)] of the second aspect of the invention, which corresponds to that shown in Figure 2a except that the three-component complex formed is subjected to a washing step before the addition of component (iv).

Full Text Amendment:

Q13

Figure 2c shows a further preferred embodiment of the second aspect of the invention, which corresponds to that shown in Figure 2a except that the three-component complex formed is subjected to a washing step before the addition of component (iv).

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Please replace paragraph 2 on page 16 with the following new paragraph 2.

Line By Line Amendment:

Figure 3a shows a preferred embodiment of the subassays (h'), (h) and (h") [of claims 7-9], wherein components (i) and (iii) are mixed in a first operation to form a two-component complex, to which component (ii) is then added in a second operation, and the resulting mixture is incubated to form a three-component complex, which is washed before adding component (iv) to form a four-component complex, which is then washed before subjecting it to chemiluminescence measurement.

Full Text Amendment:

Figure 3a shows a preferred embodiment of the subassays (h'), (h) and (h"), wherein components (i) and (iii) are mixed in a first operation to form a two-component complex, to which component (ii) is then added in a second operation, and the resulting mixture is incubated to form a three-component complex, which is washed before adding component (iv) to form a four-component complex, which is then washed before subjecting it to chemiluminescence measurement.

Please replace paragraph 3 on page 16 with the following new paragraph 3.

Line By Line Amendment:

Figure 3b shows another preferred embodiment of subassays (h'), (h) and (h") [of claims 7-9], wherein the components (i), (ii) and (iii) are added in one operation to form a three-component complex, which is then washed before adding component (iv) to form a four-component complex, which is then washed before subjecting it to chemiluminescence measurement.

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Full Text Amendment:

Figure 3b shows another preferred embodiment of subassays (h'), (h) and (h''), wherein the components (i), (ii) and (iii) are added in one operation to form a three-component complex, which is then washed before adding component (iv) to form a four-component complex, which is then washed before subjecting it to chemiluminescence measurement.

Please replace paragraph 4 on page 16 with the following new paragraph 4.

Line By Line Amendment:

Figure 3c shows a further preferred embodiment of subassays (h'), (h) and (h'') [of claims 7-9], wherein components (i) and (ii) are mixed to form a two-component complex, to which component (iii) is then added to form a three-component complex, which is washed before adding component (iv) to form a four-component complex, which is also washed before subjecting it to chemiluminescence measurement.

Full Text Amendment:

Figure 3c shows a further preferred embodiment of subassays (h'), (h) and (h''), wherein components (i) and (ii) are mixed to form a two-component complex, to which component (iii) is then added to form a three-component complex, which is washed before adding component (iv) to form a four-component complex, which is also washed before subjecting it to chemiluminescence measurement.

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Please replace the first partial paragraph on page 21 with the following new first partial paragraph.

Line By Line Amendment:

different methods using the reagents described above in the working dilutions defined in each method. The three methods used were Prior Art Method B (Fig. 1b), Method 1 according to the invention (Fig. 2a[, claim 2]) and Submethod 1 according to the invention (Fig. 3a).

Full Text Amendment:

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different methods using the reagents described above in the working dilutions defined in each method. The three methods used were Prior Art Method B (Fig. 1b), Method 1 according to the invention (Fig. 2a) and Submethod 1 according to the invention (Fig. 3a).

Please replace paragraph 2 on page 23 with the following new paragraph 2.

Line By Line Amendment:

[-oOo-]

Full Text Amendment:

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Please replace paragraph 1 on page 28 with the following new paragraph 1.

Line By Line Amendment:

Determination of specific IgE antibodies against Dermatophagoides pteronyssinus (House dust mite) allergen was performed by two different methods using the reagents described above in the working dilutions defined in each method. The two methods used were Prior Art Method A (Fig. 1a) and Method 1 according to the invention (Fig. 2a, [claim 2])

Full Text Amendment:

Determination of specific IgE antibodies against Dermatophagoides pteronyssinus (House dust mite) allergen was performed by two different methods using the reagents described above in the working dilutions defined in each method. The two methods used were Prior Art Method A (Fig. 1a) and Method 1 according to the invention (Fig. 2a)

a18

Please replace paragraph 2 on page 28 with the following new paragraph 2.

Line By Line Amendment

This method is performed on a modified version of Ciba Corning ACS:180 Benchtop Immunoassay Analyzer described in ref. 3. 25 µl of sample is dispensed by the sample probe into the cuvette and immidiately after this 100 µl of paramagnetic particles diluted 1:20 is dispensed by a fixed probe. After 8 minutes of incubation paramagnetic particles are magnetically separated and not washed. The paramagnetic particles are resuspended in 100 µl of washing buffer and 50 µl of biotinylated Dermatophagoides pteronyssinus allergen diluted 1:250 is added to the cuvette. After 10 minutes of incubation, 100 µl of lite reagent diluted 1:5000 is dispensed with a fixed probe and after additional 8 minutes of incubation the paramagnetic particles are magnetically

separated and washed 3 times with 1 ml of washing buffer. After completion of the wash cycle the paramagnetic particles are resuspended in 300 µl 0.5 g/l H_2O_2 in 0.1 M HNO_3. The cuvette enters the luminometer chamber and in front of the photomultiplier 300 µl 25 mM NaOH solution is added and the photons of light emitted are measured and quantitated and expressed as relative light units (RLU). The amount of RLU is proportional to the amount of IgE in the sample. Results

Full Text Amendment:

This method is performed on a modified version of Ciba Corning ACS:180 Benchtop Immunoassay Analyzer described in ref. 3. 25 µl of sample is dispensed by the sample probe into the cuvette and immidiately after this 100 µl of paramagnetic particles diluted 1:20 is dispensed by a fixed probe. After 8 minutes of incubation paramagnetic particles are magnetically separated and not washed. The paramagnetic particles are resuspended in 100 µl of washing buffer and 50 µl of biotinylated Dermatophagoides pteronyssinus allergen diluted 1:250 is added to the cuvette. After 10 minutes of incubation, 100 µl of lite reagent diluted 1:5000 is dispensed with a fixed probe and after additional 8 minutes of incubation the paramagnetic particles are magnetically separated and washed 3 times with 1 ml of washing buffer. After completion of the wash cycle the paramagnetic particles are resuspended in 300 µl 0.5 g/l H_2O_2 in 0.1 M HNO_3. The cuvette enters the luminometer chamber and in front of the photomultiplier 300 µl 25 mM NaOH solution is added and the photons of light emitted are measured and quantitated and expressed as relative light units (RLU). The amount of RLU is proportional to the amount of IgE in the sample. Results

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Please replace paragraph 1 on page 30 with the following new paragraph 1.

Line By Line Amendment:

[-oOo-]

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Full Text Amendment: